Docket No.: PF-0643 USN

REMARKS

Amendment to the Specification

In the Specification, Table 1, page 57 has been amended to correct a minor editorial problem in column 2. The Nucleotide SEQ ID NO: designated as "39" should instead be designated as "38". Support for this correction can be found on page 6, lines 21-23 as well as on page 28/29 of the Sequence Listing. In particular, at page 28/29 of the Sequence Listing, line <210> indicates the SEQ ID NO: as 38 and line <223> indicates the Clone ID as 5500302CB1. 5500302 is the "Clone ID" in column 3 of Table 1, and CB1 indicates the polynucleotide sequence the polynucleotide sequence of clone 5500302.

Pending claims

Claims 1-20 were originally filed in this application. By this Amendment, claims 1-20 have been canceled without prejudice or disclaimer, and new claims 21-44 have been added. The table below indicates the correspondence between the new claim(s) to the originally filed claim(s).

Original Claim(s)	New Claim(s)
1, 2	21, 22, 24, 26
3	23, 25
14	27, 28
16	29
9, 10, 11	30, 31, 43
15	32, 33
19	34
17	35, 36, 37
18	40, 41
20	42

New claim 23 is directed to an isolated polypeptide comprising the amino acid sequence of SEQ ID NO:6.

New claims 35-37 basically correspond to methods of using (claims 35 and 37) and the composition (claim 36), of the subject matter of originally filed claim 17. Note that new claims 35-37 have no counterpart in the originally filed claims, but nevertheless find support in the specification as originally filed at for example, page 32, lines 6-24.

New claims 38 and 39 recite methods of screening for a compound that specifically binds to (claim 38) or modulates the activity of (claim 39) the polypeptide of SEQ ID NO:6. New claims 38 and 39 have no counterpart in the originally filed claims, but nevertheless find support in the specification as originally filed at for example, page 19, lines 15-17 and page 44, lines 21-33.

New claims 40 and 41 basically correspond to the composition (claim 41) and methods of using (claims 40), of the subject matter of originally filed claim 18. New claims 40 and 41 have no counterpart in the originally filed claims, but nevertheless find support in the specification as originally filed at for example, page 32, lines 9-14, and page 36, line 32 through page 37, line 5.

New claim 44 is directed to a microarray containing at least one element of claim 43. Support for this claim can be found throughout the Specification, for example, page 17, lines 4-6, page 18, lines 11-33, page 43, lines 17-27, and Example VII, page 51.

Please note that the originally filed claims directed to the vectors, host cells and methods of producing the polynucleotides of SEQ ID NO:20-38 (old claims 4-8 and 12-13) are not contained in the set of new claims. Applicants expressly state that these claims are not being pursued in order to expedite prosecution of the new claims and **not** for reasons related to patentability, and are in fact fully supported by the Specification as filed. Applicants expressly reserve the right to reinstate these claims or to add other claims during prosecution of this application or a continuation or divisional application. Applicants expressly do not disclaim the subject matter of any invention disclosed herein which is not set forth in the instantly filed new claims.

Restriction Requirement

Applicants respectfully bring to the Examiner's attention that there are 19 polypeptide sequences (SEQ ID NO:1-19) and 19 polynucleotide sequences (SEQ ID NO:20-38) in the instant application. If the Examiner, in establishing a separate group for each of the polypeptide and polynucleotide sequences, intended to require Applicants to elect a single polypeptide or polynucleotide sequence within one of the eight overall groupings of the 158 groups, then the instant application comprises **152** total groups (8 x 19 = 152):

Groups 1-19 remains	Groups 1-19, comprising SEQ ID NOs:1-19, respectively, fragments.
Groups 20-38 remains	Groups 20-38, comprising SEQ ID NOs:20-38, respectively.
Groups 39-58 is really	Groups **39-57**, comprising SEQ ID NOs:20-38, respectively.
Groups 59-78 is really	Groups **58-76**, antibodies to SEQ ID NOs:1-19, respectively.
Groups 79-98 is really	Groups **77-95**, agonists of SEQ ID NOs:1-19.
Groups 99-118 is really	Groups **96-114**, antagonists of SEQ ID NOs:1-19.
Groups 119-138 is really	Groups **115-133**, methods with SEQ ID NOs: 20-38.
Groups 139-158 is really	Groups **134-152**, methods with an antagonist of SEQ ID NOs: 1-19.

Therefore, Applicants election will be made from the presence of 8 super groups, which within each are 19 sequence groups, for a total of 152 groups in designating their election.

Applicants hereby elect, with traverse, to prosecute Group 6, which includes and is drawn to at least new claims 21, 22, 23 and 28-29 directed to SEQ ID NO:6. **Further, Applicants elect, with traverse, to prosecute claims related to the polynucleotide sequences encoding the polypeptide sequence of SEQ ID NO:6, which sequences include SEQ ID NO:25, and which sequences read on claims 23, 25, 26, 30 and 31, directed to SEQ ID NO:25. Applicants traverse both the restriction requirement and the obligation to elect a single sequence for prosecution which were imposed in the Office Action faxed July 11, 2003 for at least the following reasons.**

Applicants reserve the right to prosecute the subject matter of non-elected claims in subsequent divisional applications.

I. The unity of invention standard *must* be applied to the present application

A. The present application is a national stage application

The instant application is a national stage application. In a letter mailed 1/30/2003, the USPTO notified applicants that U.S. Serial No. 09/831,805 was accepted as an application under 35 U.S.C. 371, and is ACCEPTED for national patentability examination in the United States Patent and Trademark Office.

Section 200 of Manual of Patent Examining Procedure (original 8th edition, published August, 2001) (hereinafter "MPEP") provides:

> Non provisional and provisional applications are national applications. Treatment of >a< national *>application< under U.S.C. 111 and >a< national stage **>application (a national application which entered the national stage from an international application after compliance with 35 U.S.C. 371)< are similar but not identical. Note the following examples:
>
> (A) Restriction practice under MPEP § 806+ is applied to national applications under 35 U.S.C. 111(a) while ***unity of invention practice under MPEP Chapter 1800 is applied to national stage applications***. . . .(emphasis added)

Id at page 200-2.

B. Unity of Invention *must* be applied in national stage applications

Section 1850 of the MPEP provides:

> . . . [W]hen the Office considers international applications . . . during the national stage as a Designated or Elected Office under 35 U.S.C. 371, PCT Rule 13.1 and 13.2 will be followed when considering unity of invention of claims of different categories without regard to the practice in national applications filed under 35 U.S.C. 111 . . .
>
> In applying PCT Rule 13.2 to . . . national stage applications under 35 U.S.C. 371, examiners should consider for unity of invention all the claims to different categories of invention in the application and permit retention in the same application for searching and/or preliminary examination, claims to the categories which meet the requirements of PCT Rule 13.2 . . .

Id at page 1800-60 to -61.

MPEP section 1893.03(d) reiterates the Examiner's obligation to apply the Unity of Invention standard PCT Rule 13.2 instead of U.S. restriction/election of species practice:

> Examiners are reminded that unity of invention (not restriction) practice is applicable . . . in national stage (filed under 35 U.S.C. 371) applications.

Id at page 1800-149, column 1.

II. Specific provisions of the Administrative Regulations Under the PCT and the corresponding provisions of the MPEP strongly support a finding of unity of invention among all of the claims in the present case

A. Unity of Invention is accepted as between claims to polypeptide sequences and claims to the polynucleotide sequences which encode them

Example 17, Part 2 of Annex B to the Administrative Instructions Under the PCT provides that unity of invention is accepted as between claims to polypeptide sequences and claims to polynucleotide sequences encoding those polypeptides. Those Examples are cited in MPEP section 1893.03(d) at page 1800-149, column 2 ("[n]ote also examples 1-17 of Annex B Part 2 of the PCT Administrative Instructions . . . ")

Thus, in the present case, unity of invention exists at least as between claims drawn to polypeptide sequences SEQ ID NO:1-19 (*i.e.*, claim 21) and as to claims drawn to polynucleotide sequences which encode those polypeptides (*i.e.*, claim 30).

Therefore, Applicants respectfully request that the Examiner withdraw the Restriction Requirement at least as to claims 21 and 30, and examine those claims in a single application.

B. Unity of invention exists with respect to dependent claims in the same claim category as the independent claim from which they depend

MPEP section 1850(A) and 1893.03(d), which recite the provisions of paragraph (c) of Part 1 (entitled "Instructions Concerning Unity of Invention") of Annex B (entitled "Unity of Invention") to the Administrative Instructions Under the PCT, provides:

(A) Independent and Dependent Claims.

Unity of invention has to be considered in the first place only in relation to the independent claims in an international application and not the dependent claims. By "dependent" claim is meant a claim which contains all the features of another claim and is in the same category of claim as that other claim (the expression "category of claim" referring to the classification of claims according to the subject matter of the invention claimed for example, product, process, use or apparatus or means, etc.).

(i) If the independent claims avoid the prior art and satisfy the requirement of unity of invention, no problem of lack of unity arises in respect of any claims that depend on the independent claims. In particular, it does not matter if a dependent claim itself contains a further invention . . . .

See MPEP section 1850(A) at page 1800-61. See also MPEP Appendix AI at page 53.

In the present case, claims 24, 32, 33, 36, and 41, all of which depend from claim 21 or 22, are all directed to compositions of matter, *i.e.*, to products. All of these claims contain all of the features of the independent claim. Further, as discussed above, there is unity of invention as between claim 21 and claim 30.

Thus, it is improper to restrict claims 21, 22 and 24 from claims 23, 25, 26, and 30-33, as the Examiner has done. Therefore, Applicants respectfully request that the Examiner withdraw the Restriction Requirement at least as to the composition of matter claims, and that at least those claims be considered together in a single application.

III. Unity of invention exists as between all of Applicants' claims

MPEP 1850 provides:

Unity of invention exists only when there is a technical relationship among the claimed inventions involving one or more special technical features. The term "special technical features" is defined as meaning those technical features that define a contribution which each of the inventions considered as a whole, makes over the prior art. The determination is made based on the contents of the claims as interpreted in light of the description and drawings. Annex B also contains examples concerning unity of invention.

Id at page 800-61.

MPEP 1893.03(d) similarly provides:

A group of inventions is considered linked to form a single general inventive concept where there is a technical relationship among the inventions that involves at least one common or corresponding special technical feature. The expression special technical features is defined as meaning those technical features that define the contribution which each claimed invention,

> considered as a whole, makes over the prior art. For example, a corresponding technical feature is exemplified by a key defined by certain claimed structural characteristics which correspond to the claimed features of a lock to be used with the claimed key. Note also examples 1-17 of Annex B Part 2 of the PCT Administrative Instructions as amended July 1, 1992 contained in Appendix AI of the MPEP.

Id at page 1800-149.

In the present case, unity of invention exists among all of Applicants' claims. The claimed polypeptide sequences and the claimed polynucleotide sequences encoding them are corresponding technical features which are common to all of Applicants claims, which serve to technically interrelate all of Applicants' claims, and which define the contribution over the prior art made by each of them. Thus, Applicants' claims are linked to form a single general inventive concept, and Applicants are therefore entitled to prosecute all of their pending claims in a single national stage application.

A. <u>The claimed polypeptide sequences, and the claimed polynucleotide sequences encoding those polypeptide sequences, are corresponding technical features that are common to all of Applicants' claims and that serve to technically interrelate them</u>

Applicants' claims recite *inter alia* the polypeptides SEQ ID NO:1-19, and polynucleotides encoding those polypeptides, which sequences include the polynucleotide sequences SEQ ID NO:20-38. See Table 1 of the specification. Applicants respectfully submit that the claimed polypeptide sequences SEQ ID NO:1-19, and the claimed polynucleotide sequences encoding them, are corresponding technical features, given that the former are encoded by the latter, and conversely, the latter encode the former.

Further, the claimed polypeptide and corresponding polynucleotide sequences are common to all of Applicant's claims, given that each claim refers to one or both either explicitly or implicitly, by virtue of depending from a claim which makes an explicit reference to the claimed sequences.

Moreover, the claimed polypeptide and corresponding polynucleotide sequences serve to technically interrelate all of Applicants' claims. Applicants' composition of matter claims (21-26, 30-33, 36, 41 and 43) are drawn to either the sequences themselves (21, 22, 24, 32-33, and 36 drawn to polypeptide sequences, and 23, 25, 26, 30-33 and 43, drawn to polynucleotide sequences), to

compositions of matter which comprise the sequences as one element (32, 33, 36 and 41, drawn to pharmaceutical compositions), or to compositions of matter wherein the claimed sequences functionally limit the claimed subject matter (claim 29, drawn to antibodies which specifically bind a polypeptide of claim 22).

IV. Regardless of whether the Unity of Invention standard is applied, a simultaneous search of both the claimed polynucleotides and the claimed polypeptides which they encode would not impose an undue burden on the Examiner

A. The polypeptide of SEQ ID NO:6 is encoded by the polynucleotide of SEQ ID NO:25, and is recognized in the art as such

Applicants enclose the Arrate, M.P. et al. article (M.P. Arrate, et al., Cloning of Human Junctional Adhesion Molecule 3 (JAM3) and Its Identification as the JAM2 Counter-receptor, J. Biol. Chem. (2001) 276:45826-45832). The Arrate, M.P. et al. article discloses the human junctional adhesion molecule 3 (JAM3) cDNA (GI 13448824) and protein (GI 13448825). The disclosed Arrate, et al. cDNA and protein would be recognized by one of skill in the art to be a very similar polynucleotide (GI 13448824) and a very similar polypeptide encoded by this very similar polynucleotide to SEQ ID NO:25 and SEQ ID NO:6, respectively (See enclosed polynucleotide and polypeptide alignments, Exhibits A and B, respectively). Arrate et al. also disclose the expression of this very similar polypeptide, its function as a mediator of JAM2 adhesion to T cells, and the mapping of this very similar polynucleotide to 11q25.

Accordingly, this article demonstrates that examining the prior art for the polypeptides together with the polynucleotides would involve substantially the same subject matter/sources and would not impose an undue burden on the Examiner.

B. All of the claimed polypeptide and polynucleotide sequences are corresponding technical features which are common to all of Applicants' claims and which serve to technically interrelate them

In Applicants' method claims 27, 28, 34, 35, 37-40 and 42, the claimed sequences serve as either the product of the claimed method (claims 27 and 28, drawn to a method of polypeptide production) and/or as a reagent for performing the method (claims 34, 37 and 42, 35, 38 and 40, and 39), drawn, respectively, to methods of treating a disease or condition, screening for agonists, antagonists, compounds which specifically bind, or compounds which modulate the activity of a polypeptide of claim 21 or 22.

Therefore, the claimed polypeptide and polynucleotide sequences are corresponding technical features which are common to all of Applicants' claims, and which serve to technically interrelate them.

The Election of Species Requirement

Applicants elect, with traverse, to prosecute claims related to the polypeptide sequences encoded by the polynucleotide sequence of SEQ ID NO:25, which sequences include SEQ ID NO:6. Those polypeptide sequences read on claims 21, 22, 24, 30, 31, and 43. Applicants traverse the Election of Species Requirement for at least the following reasons.

I. Members of a Markush Group which qualify as "alternatives of a similar nature" must be examined together

MPEP 1850 provides, in the section entitled "Unity of Invention - Nucleotide Sequences," that "[n]ucleotide sequences encoding the same protein are considered to satisfy the unity of invention standard and will continue to be examined together." See page 1800-65, column 1.

Section D of MPEP section 1850, which recites the provisions of paragraph (f) of Part 1 (entitled "Instructions Concerning Unity of Invention") of Annex B (entitled "Unity of Invention") to the Administrative Instructions Under the PCT, provides:

> ***D. "Markush Practice"***
> The situation involving the so-called Markush practice wherein a single claim defines alternatives (chemical or non-chemical) is also governed by PCT Rule 13.2. In this special situation, the

requirement of a technical interrelationship and the same or corresponding special technical features as defined in PCT Rule 13.2, shall be considered to be met when the alternatives are of a similar nature.

(i) When the Markush grouping is for alternatives of chemical compounds, they shall be regarded as being of a similar nature where the following criteria are fulfilled:

(A) All alternatives have **a common property or activity; AND**

(B)(1)A common structure is present, *i.e.*, **a significant structural element is shared by all of the alternatives; OR**

(C)(2)In cases where the common structure cannot be the unifying criteria, **all alternatives belong to a recognized class of chemical compounds** in the art to which the invention pertains.

(ii) In paragraph (B)(1), above, the words "significant structural element is shared by all of the alternatives" refer to cases where the compounds share **a common chemical structure** which **occupies a large portion of their structures**, or in case the compounds have in common only a small portion of their structures, the commonly shared structure **constitutes a structurally distinctive portion** in view of existing prior art. The structural element may be **a single component OR a combination of individual components linked together.**

(iii) In paragraph (C)(2), above, the words "recognized class of chemical compounds" mean that there is an expectation from the knowledge in the art that members of the class will behave in the same way in the context of the claimed invention. In other words, each member could be substituted one for the other, with the expectation that the same intended result would be achieved.

(iv) The fact that the alternatives of a Markush grouping can be differently classified shall not, taken alone, be considered to be justification for a finding of a lack of unity of invention.

(v) When dealing with alternatives, if it can be shown that at least one Markush alternative is not novel over the prior art, the question of unity of invention shall be reconsidered by the examiner. Reconsideration does not necessarily imply that an objection of lack of unity shall be raised.

See MPEP at pages 1800-61 to -62.

II. Several of the polypeptide sequences claimed by Applicants are alternatives of a similar nature, and should therefore be examined in a single application

A. SEQ ID NOS: 1, 5, 9, 10, 12 and 13 are alternatives of a similar nature

Applicants respectfully submit that SEQ ID NOS: 1, 5, 9, 10, 12 and 13 are alternatives of a similar nature in that all have been identified by Applicants as kappa L-chain immunoglobulins (hereinafter "Ig Ks") on the basis of their exhibiting significant sequence homology to known Ig Ks

and/or on the basis of the presence of certain characteristic signature sequences, motifs and domains. See Table 2 of Applicants' specification. As such, they share the common property/activity of being immunoglobulin proteins involved in the immune response.

The preceding sequences also share significant structural elements, in that all of these sequences exhibit one or more Ig domains and a signal peptide sequence. In particular, members of the Ig superfamily contain one or more repeats of a conserved structural Ig domain (in this regard, see the Specification, page 1, lines 16-21). This motif is present in all polypeptide sequences of the instant application.

B. SEQ ID NOS: 7 and 11 are "alternatives of a similar nature"

Additionally, Applicants respectfully submit that SEQ ID NOS: 7 and 11 are also alternatives of a similar nature in that all have been identified by Applicants as an Ig heavy chain variable region protein (hereinafter "Ig Hs") on the basis of their exhibiting significant sequence homology to known Ig Hs and/or on the basis of the presence of certain characteristic signature sequences, motifs and domains. See Table 2 of Applicants' specification. As such, they share the common property/activity of being immunoglobulin proteins involved in the immune response.

Therefore, SEQ ID NOS: 7 and 11 are alternatives of a similar nature which should be examined together in a single application.

Therefore, Applicants respectfully request that the Examiner withdraw the Election of Species requirement, and examine together those claims which relate to SEQ ID NOS: 1, 5, 9, 10, 12 and 13, or in the alternative, those claims which relate to SEQ ID NO:7 and SEQ ID NO:11.

C. All of the polypeptide sequences claimed by Applicants qualify as "alternatives of a similar nature"

In the alternative, all of the polypeptide sequences claimed by Applicants satisfy the PCT test, given that all possess a signal peptide sequence necessary for IG secretion, an additional structural

characteristic establishing the polypeptide sequences as members of the immunoglobulin (Ig) superfamily of proteins.

Therefore, SEQ ID NOS: 1, 5, 9, 10, 12 and 13 are alternatives of a similar nature which should be examined together in a single application.

Rejoinder

Claim 36 is a product by process claim depending from the method of use claim (claim 35) which should be rejoined and examined in compliance with Commissioner's Notice in the Official Gazette of March 26, 1996, entitled "Guidance on Treatment of Product and Process Claims in Light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)." Therefore, claim 36 should also be examined along with claims 21, 22, 24 and 32-33 directed to SEQ ID NO:6.

The method claims of claims 27-28, 34-35 and 37-39 are entitled to rejoinder upon allowance of a product claim per the Commissioner's Notice in the Official Gazette of March 26, 1996, entitled "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)" which sets forth the rules, upon allowance of a product claim, for rejoinder of process claims covering the same scope of products: See also M.P.E.P. 821.04 as follows:

> Where product and process claims drawn to independent and distinct inventions are presented in the same application, applicant may be called upon under 35 U.S.C. 121 to elect claims to either the product or process. . . The claims to the nonelected invention will be withdrawn from further consideration under 37 C.F.R. 1.142. . . . However, if applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims which depend from or otherwise include all the limitations of the allowable product claim will be rejoined.

Applicants also traverse on the grounds that the Examiner could also examine claims 27-28 and 34-39, directed to methods of using the polypeptides of claim 22. The method claims are directed to a product (i.e., the polypeptides of claim 22), which are of the same scope as the claimed polypeptides to be searched by the Examiner. Therefore, a search of the claimed polypeptides would substantially overlap examination of method claims 27-28 and 34-39 and would not be an undue burden on the Examiner.

Additionally, Applicants traverse the Restriction Requirement as between Group 6 and Group 63 (drawn to the polypeptides of SEQ ID NO:6 and antibodies to the SEQ ID NO:6 polypeptide, respectively), and hence Group 25. The claims of these groups could be examined at the same time, also without an undue burden on the Examiner. A search of the prior art to determine the novelty of the antibodies would substantially overlap with a search of the claims directed to the polypeptides. Thus, Applicants submit that examining the prior art for the polypeptides together with the antibodies would involve substantially the same subject matter and would not impose an undue burden on the Examiner.

Accordingly, as submitted above, a search of the claimed polypeptides would include the claimed polynucleotides which encode the claimed polypeptides. Therefore, it is submitted that it would not be a substantial burden on the Examiner to use the results of the necessary polypeptide search to examine the polynucleotide together with the antibody claims.

Docket No.: PF-0643 USN

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. 09-0108.

Respectfully submitted,

INCYTE CORPORATION

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